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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/632,101	08/01/2003	Marco Ciufolini	065691-0332	1920

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EXAMINER	
STOCKTON, LAURA	

ART UNIT	PAPER NUMBER
1626	

DATE MAILED: 08/22/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/632,101	CIUFOLINI ET AL.	
	Examiner	Art Unit	
	Laura L. Stockton, Ph.D.	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *July 15, 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 29-60* is/are pending in the application.

4a) Of the above claim(s) *55-60* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 29-54* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *4/22/04 & 4/28/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

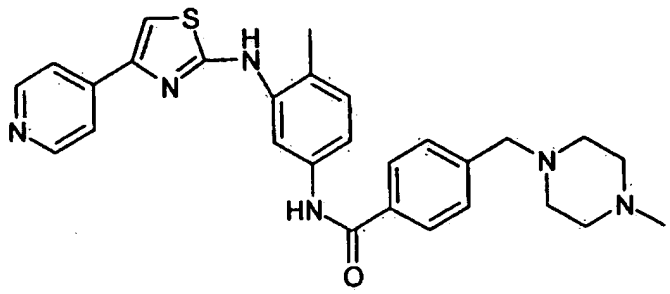
Claims 1 and 29-60 are pending in the application.

Election/Restrictions

Per an interview with Mr. Shaun Snader on July 14, 2005 (see Interview Summary - Paper No. 071405), the Examiner agreed to modify Group II (hereinafter known as modified Group II) by including R^6 representing the definition of (i). Therefore, modified Group II embraces wherein R^6 represents the definition of (i), (ii) and (iii).

Applicants' election without traverse of modified Group II, and the species of Example 80 found on pages 64-65 of the instant specification (reproduced below), in the reply filed on July 15, 2005 is acknowledged.

080: 4-(4-Methyl-piperazin-1-ylmethyl)-N-[4-methyl-3-(4-pyridin-4-yl-thiazol-2-ylamino)-phenyl]-benzamide



The requirement is still deemed proper and is therefore made FINAL.

Subject matter not embraced by modified Group II and claims 55-60 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions. Election was made **without** traverse in the reply filed on July 15, 2005.

It is suggested that in order to advance prosecution, the non-elected subject matter be cancelled when responding to this Office Action.

In accordance with M.P.E.P. §821.04 and *In re Ochiai*, 71 F.3d 1565, 37 USPQ 1127 (Fed. Cir. 1995), rejoinder of product claims with process claims commensurate in scope with the allowed product claims will occur following a finding that the product claims are allowable. Until, such time, a restriction between product claims and process claims is deemed proper. Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution to maintain either dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.**

Information Disclosure Statement

The Information Disclosure Statements filed on April 22, 2004 and April 28, 2005 have been considered by the Examiner.

Specification

It is suggested that the heading "Figure Legends", found on page 100 of the instant specification, be changed to "Brief Description of Drawings". See MPEP § 608.01(f). It is also suggested that other headings, such as those listed below, also be added to the specification.

Background of the Invention: See MPEP § 608.01(c).

Brief Summary of the Invention: See MPEP § 608.01(d).

Detailed Description of the Invention: See MPEP § 608.01(g).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 54 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. § 112, first paragraph, have been described. They are:

1. the nature of the invention,
2. the state of the prior art,
3. the predictability or lack thereof in the art,

4. the amount of direction or guidance present,

5. the presence or absence of working examples,

6. the breadth of the claims,

7. the quantity of experimentation needed, and

8. the level of the skill in the art.

The nature of the invention

Applicants are claiming a composition for treating c-kit mediated disorders comprising a compound of Claim 1 in a pharmaceutically acceptable carrier. See instant claim 54. From the reading of the specification (pages 90-96), it appears that Applicants are asserting that the embraced compounds, because of their mode action which involves the inhibition of c-kit, would be useful for treating numerous diseases and disorders such as autoimmune diseases, inflammatory diseases, CNS disorders, cancers, etc.

The state of the prior art and the predictability or lack thereof in the art

The state of the prior art is that cancer therapy, for example, remains highly unpredictable. The various types of cancers have different causative agents, involve different cellular mechanisms, and consequently, differ in treatment protocol. It is known (see Golub et al., Science, Vol. 286, October 15, 1999, pages 531-537) that the challenge of cancer treatment has been to target specific therapies to pathogenetically distinct tumor types, to maximize efficacy and minimize toxicity. Cancer classification has been based primarily on morphological appearance of the tumor and that tumors with similar histopathological appearance can follow significantly different clinical courses and show different responses to therapy (Golub et al., Science, Vol. 286, October 15, 1999, pages 531-537). There is no absolute predictability even in view of the seemingly high level

of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face. Additionally, for example, inflammation is a process that can take place in virtually any part of the body. There is a vast range of forms that it can take, causes for the problem, and biochemical pathways.

The amount of direction or guidance present and the presence or absence of working examples

The instant specification discloses *in vitro* TK inhibition assay, *ex vivo* TK inhibition assay and c-kit WT and mutated c-kit(JM) assay on pages 96-98. That a single class of compounds can be used to treat all the diseases and disorders embraced by the composition of claim 54 is an incredible finding for which Applicants have not provided supporting evidence. Applicants have not provided any competent evidence or disclosed tests

that are highly predictive for the pharmaceutical use for treating all conditions by the instant claimed compositions.

The breadth of the claims

The breadth of the claims is treating all diseases and disorders generically embraced in the composition claim language.

The quantity of experimentation needed

The nature of the pharmaceutical arts is that it involves screening *in vitro* and *in vivo* to determine which compositions containing the compounds exhibit the desired pharmacological activities for each of the diseases and disorders embraced by instant claim 54. The quantity of experimentation needed would be undue when faced with the lack of direction and guidance present in the instant specification in regards to testing all diseases and disorders generically embraced in the claim language, and when faced with the unpredictability of the pharmaceutical art. Thus,

factors such as "sufficient working examples", "the level of skill in the art" and predictability, etc. have been demonstrated to be sufficiently lacking in the instant case for instant claim 54.

The level of the skill in the art

Even though the level of skill in the pharmaceutical art is very high, based on the unpredictable nature of the invention and state of the prior art and lack of guidance and direction, one skilled in the art could not use the claimed invention without undue experimentation.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1 and 29-54 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim

the subject matter which applicant regards as the invention.

In claim 1, under the definitions of R^1 and R^7, the phrase "and/or bearing or a pendant basic nitrogen functionality" is unclear. It would appear that something is missing.

Claim 1 is indefinite because of the phrase "pendant basic nitrogen functionality" is unclear as to its meaning. Therefore, the metes and bounds of the claims cannot be ascertained. See claim 29 for same. It is noted that the phrase "pendant basic nitrogen functionality" is defined by a few examples on page 17, lines 5-10 of the instant specification. It is suggested that these specific examples be added to the claim.

In claim 1, under the definition of R^1 {definition b)}, "groupthat" should be changed to "group that".

In claim 1, there are different definitions for the "R" variable. See definition c) under R^1 and definition

(iv) under R^7. This affects dependent claims 36, 39, 41, 42, 44, 46 and 48. See claim 29 for same.

In claim 29, R^1 representing -C(=O)**Z** lacks antecedent basis. Variables Y and Z, and their respective definitions, lack antecedent basis from claim 1. Also see claims 31 and 32 for same.

In claim 29, there are different definitions for the R_a and R_b variables.

In claim 40 (near the end of the line which is next to the last line on page 12), the compound is misspelled (i.e., mo~holin).

The third and last compounds in claim 40 lack antecedent basis. See the structures of these compounds, Compound [030] and Compound [098], on page 41 and page 76, respectively, of the instant specification.

The first compound in claim 43 lacks antecedent basis. See the structure of this compound, Compound [002], on page 20 of the instant specification.

However, structure does not fit nomenclature on page 20.

All three compounds in claim 47 lack antecedent basis. See the structure of these compounds, Compound [092] and Compound [094] on page 26 and Compound [095], on page 27 of the instant specification. It is noted that the nomenclature of the first two compounds do not fit the structure shown (i.e., "thiazole-2-yl**methyl**").

The first compound in claim 49 lacks antecedent basis. See the structure of this compound, Compound [091], on pages 25-26 of the instant specification.

The compound in claim 50 lacks antecedent basis. See the structure of this compound, Compound [129], on page 22 of the instant specification.

The first compound in claim 53 lacks antecedent basis. See the structure of this compound, Compound [009], on page 29 of the instant specification.

Because of the numerous problems, some which are noted above, with the specie claims lacking antecedent

basis, the following is requested. For newly added claims 40, 43, 45, 47, 49, 50 and 53 which have lists of compounds, it is requested that Applicants provide the corresponding compound number found on page 15 of the instant specification} from the instant specification for each compound in each claim {i.e., the compound in instant claim 33 is compound [001]. This will ensure and verify that each compound in each claim has proper antecedent basis from independent claim 1. Additionally, it would also be advantageous if Applicants list one compound per line.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re*

Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1 and 29-54 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-22 of copending Application No. 10/523,018. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claimed compounds are generically described in 10/523,018. Note claim 1 in each of the applications and especially note the compound claimed in claim 18 of 10/523,018, which is the same compound as the first compound listed in instant claim 43.

The indiscriminate selection of "some" among "many" is *prima facie* obvious, *In re Lemin*, 141 USPQ 814

(1964). The motivation to make the claimed compounds derives from the expectation that structurally similar compounds would possess similar activity (e.g., c-kit inhibitors). The motivation to make the claimed compounds derives from the expectation that the instant claimed compounds would possess similar activity to that which is claimed in the reference.

One skilled in the art would thus be motivated to prepare products embraced by the prior art to arrive at the instant claimed products with the expectation of obtaining additional beneficial products which would be c-kit inhibitors. The instant claimed invention would have been suggested and therefore, obvious to one skilled in the art.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 29, 30, 34-38 and 48 are rejected under 35 U.S.C. 102(b) as being anticipated by:

a) Lago et al. {WO 00/33842} - see, for example, the compound on page 3, line 17, the product of Scheme 2 on page 5, etc.

b) Schantl et al. {Synthetic Communications (1998), 28(8), pages 1451-1462} - see compound 4ac on page 1457;

c) Hemmi et al. {WO 96/01825} - see, for example, compound (3) on page 76, lines 13-14;

d) Dexter et al. {U.S. Pat. 3,467,666} - see, for example, the compound of Example 13 in column 9; or

e) Spivack et al. {U.S. Pat. 3,201,409} - see, for example, the compound of Example 18 in column 9.

Each of the above prior art disclose at least one compound that is embraced by the instant claimed invention. Therefore, each of the prior art references anticipate the instant claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 29-41, 44-48, 50-52 and 54 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lago et al. {WO 00/33842}, Dexter et al. {U.S. Pat. 3,467,666}, Spivack et al. {U.S. Pat. 3,201,409}, Illig et al. {U.S. Pat. 6,291,514}, Stieber et al. {U.S. Pat. 2003/0158199}, and Dhanoa et al. {U.S. Pat. 2001/0044545}, each taken alone or in combination with each other when similar activities are asserted.

Determination of the scope and content of the prior art (MPEP §2141.01)

Applicants claim substituted phenylamino-2-thiazole compounds. Lago et al.(pages 2-8; and especially the compound on page 3, line 17), Dexter et al. (columns 1-2; and especially the compound of Example 13 in column 9), Spivack et al. {column 1; and especially the compound of Example 18 in column 9}, Illig et al. (columns 4-5; Formula IV in column 17; columns 24-27; and especially the compound in column 18, lines 25-26), Stieber et al. (page 2; and especially Compound No. 17 on page 7) and Dhanoa et al. (page 3; Formula IV on

page 4; the compositions on pages 8-9; and especially compound 24 on page 6, paragraph [0120]) each teach substituted phenylamino-2-thiazole compounds that are either structurally the same as (see above 102 rejection) or structurally similar to the instant claimed compounds.

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

The difference between the prior art and some of the instant claimed compounds is that the instant claimed compounds are generically described in the prior art.

Finding of prima facie obviousness--rational and motivation (MPEP §2142-2413)

The indiscriminate selection of "some" among "many" is *prima facie* obvious, *In re Lemin*, 141 USPQ 814 (1964). The motivation to make the claimed compounds

derives from the expectation that structurally similar compounds would possess similar activity (e.g., antagonizing the myt1 kinase receptor).

One skilled in the art would thus be motivated to prepare products embraced by the prior art to arrive at the instant claimed products with the expectation of obtaining additional beneficial products which would antagonize the myt1 kinase receptor. The instant claimed invention would have been suggested and therefore, obvious to one skilled in the art. A strong case of *prima facie* obviousness has been established.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Laura L. Stockton whose telephone number is (571) 272-0710. The examiner can normally be reached on Monday-Friday from 6:15 am to 2:45 pm. If the examiner is out of the Office, the examiner's supervisor, Joseph McKane, can be reached on (571) 272-0699.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for

published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

The Official fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

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Patent Examiner
Art Unit 1626, Group 1620
Technology Center 1600

August 17, 2005